IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

CUBIST PHARMACEUTICALS, INC., Plaintiff, v. HOSPIRA, INC., Defendant.	)	Civil Action No. 12-367-GMS (CONSOLIDATED)

[CORRECTED] HOSPIRA'S PROPOSED FINDINGS OF FACT AND CONCLUSIONS OF LAW

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HOSPIRA'S WITNESSES

Dr. Steven Ebert is a Clinical Professor of Pharmacy at the University of Wisconsin and a Clinical Manager of Infectious Diseases at Meriter Hospital. Tr. 216:6-10. He oversees antibiotic therapy at the hospital, advises physicians on dosing, and devises dosing regimens. Tr. 219:25-220:20. In the 1980s, he conducted dose fractionation studies to determine the pharmacodynamic properties of daptomycin. Tr. 223:15-224:2. In all, he has around 70 publications, around 50 of which concern antibiotic pharmacokinetics and pharmacodynamics. Tr. 225:12-17.

Further, Dr. Ebert has served on the FDA Anti-Infective Advisory Committee and has been a reviewer or editor on various journals. Tr. 226:3-18.

Dr. Ebert was qualified as an expert in the field of antibiotic dosing in pharmacology with special expertise in developing antibiotic dosing and administration regimens. Tr. 226:19-227:2.

Dr. Bruce Ganem is a Professor of Chemistry at Cornell University. Tr. 114:23-115:1. In 2007, he received the American Chemical Society's Creative Invention Award for his work to create a drug called taxol through semi-synthesis. Tr. 115:24-116:11. He is also the recipient of the Esselen Award for his lab's work on biologically active compounds. Tr. 116:12-17. He has about 260 publications, 75-80 percent of which relate to stereochemistry or natural products. Tr. 115:14-18.

Dr. Ganem was qualified as an expert in the field of stereochemistry and natural products. Tr. 117:16-22.

Mr. Tim Douros is Cubist's Vice President of Intellectual Property Counsel. Tr. 200:18-20; 201:2-4. He was Cubist's 30(b)(6) witness on "stereochemistry and the characterization of stereochemistry of daptomycin," "communications with the FDA regarding purity," and "delisting and relisting the reissue patent." Tr. 203:18-204:6. He testified via deposition.

Dr. Patrick Baker is one of the inventors of the '071 patent. Tr. 194:2-6. He testified via deposition.

Dr. Manuel Debono is one of the inventors of the '071 patent. Tr. 198:6-8. He testified via deposition.

Dr. Simon Baker is the Director of Research and Development at Bioline Reagents, a company that manufactures proteins and compounds involved in molecular biology kits. Tr. 393:5-18. The company purifies more than 500 compounds per year from fermentation materials. Tr. 394:4-6.

Dr. Baker has a Ph.D in Biological Sciences from the University of Warwick in the United Kingdom. Tr. 394:17-19. He has served on the faculty at the University of London and Oxford Brookes University. Tr. 396:2-19. He has been purifying compounds for nearly 30 years and in that time has purified "hundreds" of compounds. Tr. 397:21-398:4.

Dr. Baker was qualified as an expert on purification, including the purification of fermentation products and natural proteins. Tr. 400:15-20.

Mr. Paul Lynch is listed as an inventor on the purity patents. He has a bachelor's degree in biology. Tr. 429:25-430:2. He is a Senior Product Manager at Life Technologies. Tr. 430:6-10. Mr. Lynch testified via deposition.

Dr. Gordon Rausser is the Robert Gordon Sproul Distinguished Professor at the University of California-Berkeley. Tr. 1110:5-10. He has been elected a fellow of three professional associations, and has more than 250 publications. Tr. 1110:19-1111:4. He is also a former member of the President's Council of Economic Advisers. Tr. 1112:15-18. He has testified on behalf of both branded and generic drugs, on a roughly equal basis. Tr. 1113:7-15.

Dr. Rausser was qualified as an expert in the field of economics and statistics. Tr. 1113:16–114:2.

Mr. Stuart Murray is Cubist's Senior Director of Program and Portfolio Management. Tr. 1104:16-17. He was Cubist's 30(b)(6) witness on "the sales, marketing and pricing activities of the organization." Tr. 1104:25-1105:8. He testified via deposition.

I. INTRODUCTION

1. The original patent on the daptomycin compound expired in 2002, so Cubist came to trial armed with three sets of add-on patents—the '071 patent, the dosing patents, and the purity patents. Hospira should prevail on all three sets. In fact, Cubist's own experts conceded the critical points proving that Hospira prevails—as a matter of law—on every asserted claim.

2. Cubist pinned its hopes principally on the two dosing patents, devoting most of its trial time (5 of 8 witnesses) and most of its opening statement (31 of 53 slides) to those patents. That was a tacit admission of what the evidence showed: There is no principled basis for upholding either the '071 or purity patents. And, in fact, there is no principled base for upholding the dosing patents either.

A. Dosing Patents: Invalidity Of The '967 And '689 Patents

3. To find the dosing patents invalid, the Court need look no further than the testimony of Cubist expert Dr. Joseph Guglielmo, who admitted—repeatedly—that the prior art anticipates the asserted claims of the '967 patent. The following chart tells the whole story:

'967 Claim Elements	Woodworth (1992)	'226 Patent (1987)
"administering daptomycin"	Q. We do agree, don't we, that Dr. Woodworth is discussing in his article administering daptomcyin. That's correct? A. We do. Tr. 1024:24-1025:2	Q. … We agree that the '226 patent discloses administering daptomycin. Right? A. Yes. Tr. 1046:6-10
"to a human patient in need thereof"	Q. When he is making a prediction for an effective dosing regimen for the future, he is talking about giving the drug to patients. Right? A. On his prediction, yes, he is. Q. So that would be human patients in need—who have bacterial infections who need medicine. Right?	Q. … We agree that the '226 patent discloses giving daptomycin to a human patient in need thereof. Right? A. Yes. Tr. 1046:11-14

	A. Yes. Tr. 1025:10-16	
"repeatedly"	Q. But when he makes his prediction for the future, he is talking about giving the drug repeatedly. Right? A. Yes, he is. Tr. 1025:21-23; *accord* Tr. 1026:6-12	Q. We agree that the '226 patent discloses giving daptomycin to a human patient in need thereof repeatedly. Correct. A. Agreed. Tr. 1046:15-18
"at a dosage interval of once every 24 hours"	Q. … He also talks about, expressly, let's go to the bottom first, expressly talks about a dosage interval of once a day. Right? A. Yes, he did. Q. In the abstract he also talks about a dosage interval of once a day. Right? A. He does. Tr. 1025:24-1026:5; *accord* Tr. 1026:10-16; Tr. 1040:19-1041:3	Q. But at the very least you will agree once-daily dosing is expressly disclosed here? Yes? A. It is one of those intervals, yes. Tr. 1044:21-23; *accord* Tr. 1046:19-22; Tr. 1046:23-1047:1
"wherein the dose is 4 mg/kg" (claim 16, 34)/ "wherein the dose is 6 mg/kg" (claim 17, 35)	Q. Now, we agree that Woodworth expressly discloses at least as one of his options 4 and 6 milligrams per day once a day. Right? A. He does. But he also discloses giving it twice a day as well. Tr. 1031:7-11; *accord* Tr. 1026:18-22; 1026:10-16;1031:8-12; 1038:23-1039:9	Q. So what is *expressly disclosed* as an option [in the '226 patent] is 4 and 6 milligrams per day once daily. Right? A. Yes. Tr. 1046:1-3 (emphasis added); *accord* Tr. 1046:23-1047:1; 1045:15-21
Wherein it "minimizes skeletal muscle toxicity"	Q. If you gave the same dose [4 and 6 mg once daily] back in 1998 in the prior art, whether somebody knew it or not, it would *inherently minimize skeletal muscle toxicity*. Right? A. If you gave it to a patient in '98 it would do the same thing you would expect in a patient in 2014.	Q. I want to focus just on that one express disclosure, 4 milligrams once a day and 6 milligrams once a day. Would you agree with me that when you give either 4 or 6 once a day that that minimizes skeletal toxicity? A. We know that today, yes. Q. And even though they didn't know it back in 1987, had

	Tr. 1028:12-16 Q. … If you had given anywhere from 3 milligrams a day to 12 milligrams per kilogram per day once a day back in 1987, whether you knew it or not, you would in fact be minimizing skeletal muscle toxicity. True? A. True. Tr. 1049:17-21; *accord* Tr. 1047:2-11	they administered that expressly disclosed dose once a day, it would have minimized skeletal muscle toxicity. True? A. It would have minimized skeletal muscle toxicity even in that day if given that way. Tr. 1047:2-11; *accord* Tr. 1028:13-17; 1049:17-21

4. As it turns out, Dr. Guglielmo originally denied anticipation only because he applied the wrong legal standard. He did not "understand that subject matter can be inherently disclosed irrespective of whether a POSA recognized that limitation in the prior art." Tr. 1030:10-14. And he did not even know "the difference between whether … a limitation is inherently disclosed … or … expressly disclosed." Tr. 1031:3-6.

5. Dr. Guglielmo continued to apply the wrong legal standard at trial, admitting he had "difficulty" accepting anticipation "if an article expressly discloses one option that inherently" includes all elements when the article *also* discloses "some other option" that "doesn't inherently" anticipate. Tr. 1032:11-22. But Dr. Guglielmo's "difficulty" is irrelevant. Under binding authority, if the prior art discloses one anticipating option, the claim is invalid regardless of whether other "alternatives are also disclosed." *Perricone v. Medicis Pharmaceutical Corp.*, 432 F.3d 1368, 1376 (Fed. Cir. 2005). "[T]he disclosure of multiple examples" does not "render[] one example less anticipatory." *Leggett & Platt v. VUTEk*, 537 F.3d 1349, 1356 (Fed. Cir. 2008). Thus, it is irrelevant that the prior art "also disclosed" the non-anticipating "alternative" of dosing more than once a day. Express disclosure of the once-daily option still anticipates.

6. Aware of this difficulty, Cubist focused heavily at trial on *why* Lilly abandoned the daptomycin project in 1992. But that "failure-of-others" argument is irrelevant to anticipa-

tion. It is also irrelevant to obviousness, because Cubist's narrow evidence (the alleged failure to find effective dosing for *S. aureus endocarditis* (SAE)) is not "commensurate in scope with the claims" (covering dosing for *all* bacterial infections). *MeadWestVaco Corp. v. Rexam Beauty & Closures, Inc*., 731 F.3d 1258, 1264-65 (Fed Cir 2013) (reversing non-obviousness ruling).

7. The other dosing patent, the '689 patent, adds nothing to this case. It claims extending the dosing interval to once every 48 hours, which is just straight math. The prior art taught that (1) daptomycin was renally-cleared, and (2) for *any* renally-cleared drug, hospitals must adjust dosing for the renally-impaired. Tr. 1090:2-11. Dr. Guglielmo conceded that the common "formula" for that adjustment required dosing of "4 to … 6 milligrams every 48 hours." Tr. 1095:10-14.

B. '071 Patent: Noninfringement vs. Written Description Dilemma

8. For the '071 patent, Cubist is caught on the horns of a dilemma. If the certificate of correction ("CoC") is invalid, then Hospira does not infringe. And if the CoC is valid, then the patent violates the written description requirement. Either way, Hospira prevails.

9. First, a CoC may not "broaden[]" a claim to the point that the "new version covers territory that the old one did not." *Central Admixture Pharmacy Servs., Inc. v. Advanced Cardiac Solutions, P.C.* 482 F.3d 1347, 1353 (Fed. Cir. 2007). But as Dr. Gerwick admitted on cross, it is "self-evident" that daptomycin with "D" asparagine (D-Asn) was "not covered before" the 2008 correction but "would be covered" "after the correction." Tr. 837:5-838:6. That is textbook broadening, which means the CoC is invalid and Hospira avoids infringement.

10. Second, even if the CoC *were* valid, Hospira would still prevail due to a written description violation. A patent application must "reasonably convey" to skilled scientists what the patent holder claims. *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010). But as Dr. Gerwick admitted at trial—"I guess that's true, yes"—the 1987 application did

not "reasonably convey" the now-claimed D-Asn daptmycin molecule. Tr. 834:19-23; *accord* 831:23-832:3. Thus, regardless of whether the CoC is valid, Hospira prevails.

11. As explained below, the '071 patent is invalid for yet a third independent reason: improper recapture. To obtain its original '226 patent, Eli Lilly "surrendered" subject matter that Cubist "recaptured" by obtaining the asserted claims in the reissued patent.

C. Purity Patents: Invalidity Of The '243 And '352 Patents

12. The purity patents are also invalid as a matter of law. The asserted product-by-process claims cover daptomycin with 93 to 97% purity. Cubist admitted to the patent office that the prior art disclosed 93% purity, and prior art textbooks—aimed at beginners—taught that "complete purification" can "normally be done in a short period of time." DTX-385 at 16.

13. That is exactly what happened here. Cubist achieved *99%* purity of daptomycin by running Eli Lilly's prior art material *once* through perhaps the most common purification tool—an ion exchange column. Tr. 435:16-436:12; 437:14-438:1 (Baker). And for that simple step, Cubist hired someone (Mr. Paul Lynch) who admittedly used his company's "standard approach"—the "same general types of testing as [he] would have performed in the ordinary course." Tr. 431:24-432:11, 433:16-434:9. That "standard" purification work is not a patentable invention, which is why no company other than Cubist ever named Mr. Lynch an inventor for conducting work he routinely does in the "ordinary course." Tr. 433:12-21.

14. Unable to save its patents under the "general rule" for product-by-process claims —which ignores process steps when assessing validity—Cubist attempts to shoehorn this case into a rare exception, applied by the Federal Circuit just once in the last 25 years. But that exception applies only when the claimed "process … imparts 'structural and functional differences' distinguishing the claimed product from" the product produced by the "prior art" (and obvious variants thereof). *Greenliant Sys., Inc. v. Xicor LLC*, 692 F.3d 1261, 1268 (Fed. Cir. 2012).

Cubist says its claimed "micelle filtration" step produces the requisite differences based on endotoxin and saponin levels and the general impurity profile. Tr. 92:2-93:4.

15. Not true. There were no "functional" differences. As Cubist's witnesses admitted, Lilly administered its prior art material to well over 100 patients without any ill effects from those alleged impurities. Tr. 661:11-20 (Eisenstein); Tr. 845:18-846:13, 847:2-16 (Gerwick). Nor were there any "structural" differences. That was proven in multiple ways, including the fact that—as Dr. Gerwick admitted—Lilly produced many saponin-free and endotoxin-free batches over a decade before Cubist's work. Tr. 852:22-25; 853:7-9; 857:16-858:1. The purity patents themselves disprove any purported structural differences, because the patents' examples using standard purification techniques were much purer (*every* one reaching at least 99%) than those using the allegedly novel and critical micelle filtration (*none* higher than 93%). DDX-Gerwick-011; Tr. 859:22-861:15. Dr. Gerwick admitted "I really can't tell" when asked whether there was *any* "structural and functional" difference between the two sets of examples. Tr. 865:8-13.

16. Even if the Court *were* to apply the structural/function exception, however, the claims would still be invalid. Micelle filtration was obvious. The prior art clearly disclosed that daptomycin was a "surfactant" (Tr. 485:18-487:1 (Baker)), and also expressly taught that micelle filtration can be used "for the recovery and purification of *most surfactants*." DTX-345 (Lin 1997) (emphasis added). Cubist offered no credible response to this clear proof of obviousness.

17. The purity patents are invalid for an independent reason under 35 U.S.C. § 102(f). It was Lilly, not Cubist, who first invented highly pure daptomycin. Cubist admitted to the FDA that Lilly obtained 98% pure daptomycin over a decade before Cubist's priority date. DTX-079 at 124; Tr. 417:17-418:19; 727:24-728:13; 883:21-884:12. That Cubist used another way to

make the same product is irrelevant.

D. Purity/Dosing Patents: Noninfringement vs. Written Description Dilemma

18. Cubist faces the same dilemma for the dosing and purity patents as it does for the '071 patent: the patents are either invalid for a lack of written description or not infringed.

19. This Court construed "daptomycin" as the D-Asn antibiotic by adding a process limitation to the molecule's non-stereochemical structure—specifically, an "antibiotic derived from the fermentation of Streptomyces roseoporus." D.I. 59 at 1. Under that construction, the patents violate the written description requirement for the same reasons as the '071 patent.

20. The only way to avoid that problem would be to construe "daptomycin" without a process limitation—leading to a finding of non-infringement. A district court may revise its claim construction "as its understanding of the technology evolves." *Pressure Prods. Med. Supplies, Inc. v. Greatbach, Ltd.*, 599 F.3d 1308, 1316 (Fed. Cir. 2010). And Hospira respectfully submits that, since *Markman*, both the facts and law have evolved. Contrary to this Court's *Markman* finding (urged by Cubist), correcting daptomycin's stereochemistry did not require "new technology." D.I. 59 at 2 n.1. Both parties' experts have now agreed the necessary technology was available in the late 1980's. Tr. 141:7-21 (Ganem); 841:6-842:11 (Gerwick). The law changed too, because the Federal Circuit recently held that a patentee who, as here, relies on an uncorrected scientific mistake when drafting its claims is stuck with the consequences. *See Bayer CropScience v. Dow AgroSciences*, 728 F.3d 1324, 1328-29 (Fed. Cir. 2013).

21. In the end, to attempt to salvage its patents, Cubist is urging this Court to apply an analysis that lacks intellectual rigor—one that focuses on irrelevant evidence and incorrect legal standards. The Court should decline that invitation to commit clear reversible error.[1]

[1] For the Court's information, the 30-month stay for the 500mg product expires August 7, 2014.

II. THE DOSING PATENTS ARE INVALID.

A. The '967 Patent Is Anticipated By The Woodworth Article.

1. Proposed Findings Of Fact On Woodworth

22. In 1992, the Woodworth article (DTX-427) made predictions for effectively dosing daptomycin. When Woodworth made those predictions, the prior art showed that the following two doses were safe and effective:

- **Daily doses of 2 mg/kg administered once daily**: In Lilly trials involving a total of 63 patients, this dose proved "safe and effective in patients with various gram positive infections." DTX-399 Abstract 932 (Sexton 1988).
- **Daily doses of 6 mg/kg administered as 3 mg/kg twice daily:** In trials involving 89 patients, this dose was considered both ***safe*** (only 2 of 89 patients had elevated CPK with no skeletal muscular toxicity (SMT) symptoms, leading Lilly to conclude that daptomycin was as safe as "conventional agents" (DTX-453 at 32)) and ***effective*** ("effective in [bacteremia] and [non-*S. aureus* endocarditis]." DTX-339 Abstract 885 (Lee 1991)).

23. In recommending *other* "effective" dosing regimens—a recommendation Cubist followed in its first human trial—Woodworth twice disclosed the *exact same doses at the exact same interval* as claimed in the '967 patent:

Abstract's Final Sentence	Conclusion
"On the basis of the drug's pharmacokinetics and antibacterial activity, ***doses of 4 to 6 mg/kg/day, possibly in divided doses***, are predicted to be effective." DTX-427 at Abstract (emphasis added).	". . . the drug's longer half-life, allowing ***once- or twice-daily*** administration with the proper doses. In conclusion, our data suggest that good antibacterial activity would be produced from single doses of ***4 to 6 mg/kg***." DTX-427 at 324 (emphasis added).

This clear disclosure left Dr. Guglielmo with no choice but to admit Woodworth discloses *every element* of the asserted claims of the '967 patent, as detailed in the chart above (¶ 3).

2. Proposed Conclusions Of Law On Woodworth

24. A claim is anticipated if a "single prior art reference" discloses "each and every"

claim element "either expressly or inherently." *In re Cruciferous Sprout Litig.*, 301 F.3d 1343, 1349 (Fed. Cir. 2002). "Under the principles of inherency, if the prior art necessarily functions in accordance with, or includes, the claimed limitations, it anticipates." *Id.* And "[i]nherency is not necessarily coterminous with the knowledge of those of ordinary skill in the art," who "may not recognize the inherent characteristic[]." *Id.*; *accord Perricone*, 432 F.3d at 1378.

25. Cubist offered nothing to rebut Woodworth's clear anticipation. Cubist's main argument was that Woodworth "teaches away" from the claimed invention. But "whether a reference 'teaches away' from the invention is inapplicable to an anticipation analysis." *Leggett*, 537 F.3d at 1356. The key is whether the invention is *disclosed*; "a reference is no less anticipatory if, after disclosing the invention, the reference then disparages it." *Bristol-Myers Squibb v. Ben Venue Labs.*, 246 F.3d 1368, 1376 (Fed. Cir. 2001).

26. Cubist next says Woodworth did not *actually* administer his predicted "effective" doses once-daily to patients—only to healthy volunteers in a single-dose study. Tr. 988:18-23. But the Federal Circuit has already rejected that argument, holding that "anticipation does not require actual performance of suggestions in a disclosure." *Ben Venue*, 246 F.3d at 1379.

27. Cubist alternatively focused on Woodworth's *other* disclosures when attempting to minimize Dr. Guglielmo's repeated admission that the *expressly-disclosed*, once-daily doses of 4 and 6 mg/kg would inherently minimize skeletal muscle toxicity. *See, e.g,* Tr. 1028:4-7; 1028:12-16; 1047:2-11; 1049:17-21. On both direct and redirect, for instance, Cubist argued against anticipation by emphasizing that Woodworth *also* disclosed a twice-daily option.

28. The Federal Circuit has already rejected that argument too. The law of anticipation asks whether a reference discloses the claimed invention, not "whether alternatives are also disclosed." *Perricone*, 432 F.3d at 1376. The Federal Circuit has firmly rejected "the erroneous

assumption that the disclosure of multiple examples renders one example less anticipatory." *Leggett*, 537 F.3d at 1356. Indeed, in *Perricone*, the prior art reference taught "fourteen skin benefit ingredients." 432 F.3d at 1376. Yet "the use of one … anticipate[d] [the patentee's] claims." *Id.* at 1377.

29. Lacking an answer, Cubist called Woodworth himself to say he did not "conclude that daptomycin should be dosed once daily." Tr. 618:13-16. But this carefully-crafted statement about what "should" be done—from a paid fact witness given $300 to 500 per hour for three preparation meetings and a day in court for barely 25 minutes of testimony—is irrelevant. Tr. 621:23-622:6, 622:9-10.[2] All that matters is that Woodworth's *article* expressly discloses once-daily dosing of 4 mg/kg and 6 mg/kg—a point Dr. Guglielmo repeatedly admitted. Tr. 1026:10-16; 1026:18-22; 1031:7-11; 1038:23-1039:9.

B. The '967 Patent Is Anticipated By The '226 Patent.

1. Proposed Findings Of Fact On The '226 Patent

30. The '226 patent independently anticipates. As Dr. Guglielmo admitted, that patent discloses every element of the '967 patent's asserted claims. *Supra* ¶ 3 (chart). The '226 patent was filed by Lilly in 1987 with a recommended narrow dosing range:

> A typical daily dose for an adult human is from ***about 100 mg to about 1.0 g***.
>
> In practicing this method, the antibiotic compound can be administered as ***a single daily dose*** or in multiple doses per day. DTX-002 col. 10 ln. 57-61.

31. As to the dosing interval, Dr. Guglielmo admitted that "once-daily dosing [was]

[2] It is, of course, permissible to compensate a fact witness for lost time when the "loss of economic opportunity" can be "reasonably measured." Delaware State Bar Association Committee on Professional Ethics Opinion 2003-3 at 9 (Aug. 14, 2003). For example, a full-time consultant may be compensated at his normal rate. *Id.* But Woodworth is not a full-time consultant. He has a day job at Biogen Idec, and he lost no pay for testifying. Tr. 622:11-12, 22-24. In such a case, compensation of hundreds of dollars per hour may "make the witness 'better off' than if he/she pursued other business opportunities"—a prohibited result. Ethics Opinion 2003-3 at 11 (*citing* Colorado Bar Association Ethics Committee Formal Op. 103, at *5-6).

expressly disclosed" (Tr. 1044:21-23) and further that there are only five "most common" dosing intervals for antibiotics—4, 6, 8, 12, and 24 hours. Tr. 991:16-24.

32. As to dosage amount, both experts agreed that the range of "about 100mg to about 1.0 g" for a "typical daily dose" corresponds to a narrow range of 1.4 mg/kg to 14 mg/kg under a standard conversion using a hypothetical typical 70kg human. Tr. 276:21-277:16 (Ebert); 1043:19-1044:3 (Guglielmo). And they further agreed that the prior art disclosed only "whole integer dosages" of daptomycin, and a POSA thus would "only see, as a starting point, 13 options" at each whole integer dose, including 4 mg/kg and 6 mg/kg. Tr. 1045:8-14 (Guglielmo); *accord* Tr. 277:17-279:2 (Ebert). Given these limited options, Dr. Guglielmo directly and unequivocally admitted "expressly disclosed" anticipation:

> Q. So what is expressly disclosed as an option [in the '226 patent] is 4 and 6 milligrams per day once day. Right?
>
> A. Yes.

Tr. 1046:1-3 (Guglielmo); *accord* Tr. 1046:23-1047:1; 1045:15-21.

2. Proposed Conclusions Of Law On The '226 Patent

33. As with Woodworth, Cubist has no good response to the '226 patent's anticipation. Faced with Dr. Guglielmo's repeated admission that the '226 patent "expressly disclosed" the claimed invention, Cubist responded that the key disclosure does not use the precise numbers "4" and "6." *See* Tr. 1095:23-1096:12. But the Federal Circuit recently described as "silly" the notion "that [a] reference to '5-15 mg' did not disclose all dosages between 5 and 15 mg." *Tyco Healthcare Grp. v. Mutual Pharm.*, 642 F.3d 1370, 1373 n.3 (Fed. Cir. 2011). The issue is "whether the genus was of such a defined and limited class that one of ordinary skill in the art could 'at once envisage' each member of the genus." *Wm. Wrigley Jr. Co. v. Cadbury Adams USA*, 683 F.3d 1356, 1361 (Fed. Cir. 2012). And both experts agreed a POSA would "at once

envisage" the disclosed range's 13 integers, including both 4 mg/kg and 6 mg/kg.

34. Even if the Court were to disregard Dr. Guglielmo's repeated admission that the claimed doses were "expressly disclosed," the claims would *still* be anticipated. When a claimed invention falls within a prior art range, as here, it is anticipated if "there is no allegation of criticality or any evidence demonstrating any difference across the range." *ClearValue v. Pearl River Polymers*, 668 F.3d 1340, 1345 (Fed. Cir. 2012). Dr. Guglielmo admitted that there was not:

> Q. If you had given *anywhere from 3 milligrams a day to 12 milligrams per kilogram per day once a day* back in 1987, whether you knew it or not, you would in fact be minimizing skeletal muscle toxicity. True?
>
> A. True.

Tr. 1049:17-21 (emphasis added). In other words, 4 and 6 mg/kg do not minimize skeletal muscle toxicity any differently than any other dose in the disclosed "typical" range:

35. Cubist also says the number of disclosed intervals is too large to anticipate. But the *only* expressly-disclosed interval is once-daily dosing, and there are just four other conventional intervals. The Federal Circuit has "reject[ed] the notion that" a disclosed solution "cannot anticipate because it appears without special emphasis in a longer list." *Perricone*, 432 F.3d at 1376. That rule governs here. And again, the Federal Circuit has held that disclosure of "multiple examples" does not "render[] one example less anticipatory." *Leggett*, 537 F.3d at 1356.

36. Finally, as with Woodworth, Cubist asserts that the '226 patent cannot anticipate because it does not refer to skeletal muscle toxicity. But again, an inherent disclosure occurs when "the prior art necessarily functions in accordance with" the disputed claimed limitation *Leggett*, 537 F.3d at 1354. And Dr. Guglielmo admitted that once-daily dosing of 4 or 6 mg/kg necessarily minimizes skeletal muscle toxicity. *Supra* ¶¶ 3, 27. Whether a POSA had "full recognition of those benefits" is irrelevant. *Perricone*, 432 F.3d at 1378.

C. The Dosing Patents Are Obvious

1. Proposed Findings Of Fact On Obviousness

37. Even if Cubist could avoid anticipation, the asserted claims would be obvious. Everything pointed toward extended dosing: (1) Woodworth and the '226 patent expressly disclosed the once-daily option, (2) daptomycin's known properties, (3) Lilly's clinical trials, and (4) the experience with aminoglycosides, which, as Cubist admitted to the FDA, revealed the *same* solution to the *same* problem with a *similar* drug. Cubist could unearth nothing pointing the other direction, away from once-daily dosing.

a. Both Woodworth And The '226 Patent Expressly Suggested Once-Daily Dosing.

38. The '967 patent's purported "invention" is increasing the dosing interval to at least 24 hours. As the patent states: "This long dosing interval minimizes skeletal muscle toxicity and allows for higher peak concentrations of daptomycin, which is related to daptomycin's efficacy." DTX-014 at Abstract. But that is exactly what Woodworth and the '226 patent suggest. Regardless of whether their teachings are sufficient for anticipation, the '226 patent specifically stated that once-daily dosing was a "typical daily dose." And Woodworth twice, and expressly, suggested once-daily dosing as one of only two options.

b. The Known Characteristics Of Daptomycin Pointed Toward Once-Daily Dosing.

39. The known properties of daptomycin also pointed powerfully toward once daily dosing, particularly considered in light of the published results of Lilly's clinical trials. Those trials tested two dosing regimens: (i) 2 mg/kg per day as a single daily dose, which proved "safe and effective in patients with various gram positive infections" (DTX-399 Abstract 932), and (ii) 6 mg/kg per day (given as one 3 mg/kg dose every 12 hours), which proved "effective in [bacteremia] and non-[*S. aureus* endocarditis]." DTX-339 Abstract 885; *see also* DDX-Guglielmo-013.[3]

40. The only issue that surfaced in those trials was the need to "improve" efficacy against *S. aureus* endocarditis or SAE. Toxicity was not a major concern, because only two of 89 patients who took 3 mg/kg every 12 hours had elevated CPK (DTX-339 Abstract 885)—a "marker" for skeletal muscle toxicity. Tr. 957:6-8. But no patient showed symptoms of actual skeletal muscle toxicity. Tr. 1065:8-11 (Guglielmo). Lilly itself thus concluded that daptomycin's "safety" was "similar" to other "conventional agents" (DTX-453 at 32), and Dr. Ebert agreed that "[w]hen you consider the risk-benefit, it's a pretty safe drug." Tr. 301:10-11.

41. A POSA would be motivated to use once-daily dosing to improve efficacy for SAE while minimizing the risk of higher toxicity and maintaining (or even lowering) the total daily dose of 6 mg/kg. Four known properties of daptomycin made this obvious.

42. *First*, as Dr. Guglielmo repeatedly admitted, daptomycin was known to be a concentration-dependent killer— the "higher the peak" blood concentration, the "better the killing," which suggested once-daily dosing (higher peaks) instead of dividing the dose to be administered

[3] Cubist spent an inordinate amount of trial time on a different study—a study that administered 8 mg/kg per day and showed minor SMT symptoms in two of five patients. This study is irrelevant, because, as Dr. Guglielmo admitted, it was not prior art. Tr. 1066:17-19.

more often (lower peaks). Tr. 1041:7-18 ("That is correct."); *accord* Tr. 1091:10-12 (same); 1076:17-19 (same); 1042:2-8 (admitting *in vitro* models showed concentration-dependent killing).

43. *Second*, daptomycin has a "longer half-life" (DTX-427 at 324; *accord* Tr. 243:2-7), which means the drug works in the body over a longer period. Tr. 243:14-19 (Ebert). Since antibiotics are usually dosed every 3-6 half-lives—a key principle Cubist never disputed—daptomycin's eight-hour half-life suggested a 24-hour dosing interval. Tr. 243:20-244:3 (Ebert).

44. *Third*, as Dr. Guglielmo admitted, daptomycin was known to have a long post-antibiotic effect. Tr. 1089:7-13; *see* DTX-268 at 424 (Baltz); DTX-427 at 324 (Woodworth). Like the long half-life, this effect "motivates a POSA to test longer dosing intervals." Tr. 315:1-4 (Ebert). A drug with a long post-antibiotic effect can be given less often, since it suppresses bacteria even *after* being eliminated from the body. Tr. 242:11-23; 313:13-314:1 (Ebert).

45. *Fourth*, any skeletal muscle toxicity *potentially* caused by daptomycin was known to be reversible through extended dosing. As Dr. Ebert explained, "a number of other drugs … have been identified as causing skeletal muscle toxicity, and in each occasion when the drug is removed, the toxicity is reversed." Tr. 326:6-9. Dr. Guglielmo agreed that "the majority" of skeletal muscle toxicities were reversible. Tr. 1083:25-1084:7. Standard dosing textbooks confirm that an "important consideration … is whether the interval between doses is sufficient to allow for complete repair of tissue damage." DTX-282 at 16. This too counsels a longer dosing interval, so the muscles have more time to repair themselves before the drug is reintroduced.

46. These characteristics of daptomycin—concentration-dependent killing, a long half-life, a long post-antibiotic effect, and reversible toxicity—all pointed towards once-daily dosing. Tr. 242:11-23; 243:20-244:19; 313:20-314:1; 314:10-315:4; 324:7-16; 329:15-19.

c. The Art On Aminoglycosides Pointed Toward Once-Daily Dosing.

47. So did clinical experience with aminoglycosides. Clinicians used the *same* solution as Cubist (once-daily dosing) to defeat the *same* problem (reversible toxicity) in a *similar* drug (aminoglycosides and daptomycin share three key properties). DTX 270 at 32 (Barclay).

48. In addition to causing a reversible toxicity, the key "factors" scientists identified as supporting "larger doses of aminoglycosides … given less frequently" were that "[a]minoglycosides display concentration-dependent bacterial killing" and "have a long postantibiotic effect." DTX 270 at 32 (Barclay 1994). Both experts agreed daptomycin shared these properties:

- *Concentration-dependent killing*. Tr. 319:5-19 (Ebert); 1088:5-1089:13 (Guglielmo).
- *Long post-antibiotic effect*. Tr. 319:5-19 (Ebert); 1088:5-1089:13 (Guglielmo).
- *Reversible toxicity*. Tr. 319:5-19 (Ebert); 1082:21-1084:7 (Guglielmo).

49. One need not speculate about any of this. Cubist's own patents admitted that aminoglycosides had "been administered as a high dose at less frequent intervals rather than at lower doses at more frequent intervals in order to reduce their toxicity." DTX-014, col. 2 ln. 61-65; *see also* Tr. 320:9-321:4 (Ebert discussing this passage). Cubist told FDA the same thing, emphasizing that once-daily dosing for daptomycin was "not unique:"

> Once-daily administration is hypothesized to lead to less time above a toxic threshold plasma concentration, and therefore greater time between doses for repair of subclinical muscle damage associated with daptomycin. These results suggest that appropriate adjustment of dosing schedule can minimize daptomycin skeletal muscle toxicity, and that a dose regimen of 6 mg/kg/day, administered as a single daily dose, is likely to be as safe as 3 mg/kg q12h. *These observations on the relationship between dosing interval and toxicity are not unique to daptomycin. Once-daily dosing has also been demonstrated to decrease the nephrotoxicity induced by aminoglycoside antibiotics in animals and man.*

DTX-029 at CUB00120415 (emphasis added); Tr. 1087:3-1088:4 (Guglielmo discussing this passage). This admission is unqualified—and thus tantamount to an admission of obviousness.

50. Cubist was not so candid with the patent office. Its patent specification argued that the aminoglycoside art would *not* have suggested once-daily dosing for daptomycin because the two drugs cause different kinds of "toxicity" with different "mechanisms" at different "sites." DTX-014, col. 2 ln. 66-col 3 ln 5. That is true, but irrelevant. As Dr. Guglielmo admitted, it was known that the "majority" of *both* toxicities were "reversible." Tr. 1082:21-1084:7. And he never provided a cogent reason why a POSA would look beyond that similarity.

51. In a misleading passage, Cubist's patent specification identified other irrelevant "differences" between aminoglycosides and daptomycin:

> In addition, aminoglycosides are structurally dissimilar to daptomycin,[4] act only on gram-negative bacteria,[5] have a different mechanism of antibacterial action from daptomycin[6] and exhibit different mechanisms of resistance.[7]

DTX-014 col. 3 ln. 5-9. As confirmed by the footnoted testimony, Dr. Guglielmo admitted *each one* was irrelevant to determining a dosage regimen to address toxicity. Dr. Ebert agreed. Tr. 329:11-14.

d. Nothing In The Art Taught Away From Once-Daily Dosing.

52. Contrary to Cubist's view, nothing in the art taught away from once-daily dosing.

53. ***Woodworth***. Cubist says Woodworth teaches away from once-daily dosing based on a few lines about *a third party's* study, which Woodworth states had "assume[d] an initial unbound daptomycin concentration" corresponding "to a dose of 20 to 25 mg/kg, which is presently an unrealistic dose." DTX-427 at 324. As Dr. Guglielmo admitted (Tr. 1037:22-1038:1),

[4] Tr. 1085:6-10 (agreeing that this would not be relevant to "whether or not to analogize daptomycin and aminoglycosides").

[5] Tr. 1085:24-1086:6 ("I agree" that "that is not a reason for a POSA to decline to analogize aminoglycosides").

[6] Tr. 1086:7-13 (same admission).

[7] Tr. 1086:14-19 (same admission).

Woodworth was saying that *20-25 mg/kg* was an "unrealistic *dose*" (DTX-427 at 324 (emphasis added)), not that *once-daily dosing* was an "unrealistic" *interval*. In fact, as noted, Woodworth twice expressly recommended once-daily dosing.

54. Indeed, the very next sentence of Woodworth's article references *another* study, which he said was "*modeled correctly*" and "used *concentrations closer to those anticipated* from multiple dosing of *6 mg/kg*" (DTX-427 at 324 (emphasis added); *see also* DDX-Guglielmo-019)—the very dose recommended "in the abstract and in the conclusion." Tr. 1038:23-1039:1 (Guglielmo: "Yes."). Thus, Woodworth is saying only that a high dose of 20-25 mg/kg is "unrealistic" (Tr. 1037:22-1038:1 (Guglielmo)), but a dose of 6 mg/kg is feasible—which is why he recommended that once-daily dose.

55. ***Baltz.*** Dr. Guglielmo also said that Baltz's review article taught away from once-daily dosing. But Dr. Guglielmo relied on Baltz's description of two *other* articles that Dr. Guglielmo admittedly "did not read … at that time" (Tr. 1068:18-1069:2, 1071:10-25)—even though he admitted that a POSA would "absolutely … pull the original reference" "when important in a review article." Tr. 1070:9-25. After actually reading those articles, Dr. Guglielmo was forced to admit that "[i]n my opinion, both of these studies you mentioned don't teach for or against the use of daptomycin given every 24 hours." Tr. 1072:18-20.

56. ***Lee abstract***. Dr. Guglielmo changed his opinion on the Lee abstract too, finally admitting that this reference "makes no conclusion one way or the other" about once-daily dosing. Tr. 1077:17-1078:1. In fact, this abstract encourages the claimed invention. It expressly teaches that "[h]igher doses of [daptomycin] may be necessary to achieve improved success rates in SAE." DTX-339 Abstract 885. As Dr. Guglielmo admitted, this teaching is not limited to increasing the *daily* dose of 6 mg/kg and, instead, gives the option of increasing the *individual dose*

of 3 mg/kg. Tr. 1076:3-5. This leads *directly* to the claimed invention because the claimed doses of 4 mg/kg and 6 mg/kg are both higher than Lee's. Tr. 1076:6-13.

57. In sum, a POSA would have known that daptomycin had all the characteristics of a drug suitable for once-daily dosing, and nothing in the art taught away from that solution.

e. The '689 Patent Adds Nothing To This Case.

58. The '689 patent adds nothing to this dispute, as evidenced by how little trial time Cubist spent on it. Dr. Guglielmo discussed the patent in the most cursory way, and Cubist even forgot to elicit a formal obviousness opinion until *redirect*. *See* Tr. 1099:14-1101:2.

59. The '689 patent is identical to the '967 patent, except that it extends the dosing interval to 48 hours. That interval is relevant only to patients with compromised kidney function ("renally-impaired"), and both Cubist's and Hospira's labels call for dosing once every 48 hours.

60. The claimed 48-hour dosing "invention" is nothing more than straight math from the prior art, which taught the POSA all she needed to know. *First*, daptomycin was primarily cleared from the body via the kidneys—78% according to Woodworth. Tr. 1090:2-7 (Guglielmo); DTX 427 at Abstract (Woodworth).

61. *Second*, there were only two ways to adjust a dosing regimen for a renally-cleared drug in a renally-impaired patient: increase the dosing interval or decrease the dose, which both experts agreed was well known in the art. Tr. 332:23-335:21 (Ebert); 1090:12-1091:9 (Guglielmo); DTX-371 at 45 (Mutschler 1995); DTX-355 at 785 (McKindley 1998); DTX-312 at 681-82 (Freeman 1997); DTX-392 at 215-16 (Rotschafer 1988).

62. *Third*, if the drug in question is a concentration-dependent killer (like daptomycin or aminoglycosides), increasing the interval was preferred to take advantage of the higher killing power from the higher peak concentration. For instance, the Freeman article taught that "[i]f one is to adhere to the principles of high-dose, less frequent aminoglycoside dosing therapy, it would

seem more logical to maintain a fixed dose and lengthen the interval . . . ." DTX-312 at 682. Both experts agreed this was known in the art. Tr. 335:6-336:19 (Ebert); 1092:7-1093:6 (Guglielmo); DTX-270 at Abstract (Barclay); DTX-312 at Abstract (Freeman); DTX-290 at 48 (Craig 1995).

63. *Fourth*, adjusting the dosing interval requires nothing more than basic math. As Dr. Ebert explained, hospitals routinely double a dosing interval for patients with 50% kidney function, and have been doing so since at least 1990. *See* Tr. 338:7-13 (discussing DTX-355 (McKindley 1998)); Tr. 338:25-339:6. As Dr. Guglielmo admitted, a standard calculation based on Woodworth would lead a POSA directly to the claimed 48 hour dosing interval:

> Q. I take Woodworth's 4 to 6 milligrams once a day, and I give it to someone who has a 50-percent drop in renal function. If I followed McKindley's formula, I would give them 4 to have 6 milligrams every 48 hours. Correct?
>
> A Correct, according to McKindley.

Tr. 1095:10-14. The conclusion is inescapable: Woodworth's disclosure *automatically* discloses extending the dosing to 48 hours for the renally-impaired through *simple arithmetic*.

2. Proposed Conclusions Of Law On Obviousness

64. Where, as here, "there is a design need or market pressure to solve a problem [improving SAE efficacy] and there are a finite number of identified, predictable solutions [increasing the dosing interval to increase both killing power and tissue recovery time], a person of ordinary skill has good reason to pursue the known options [once-daily dosing] within his or her technical grasp." *KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398, 421 (2007). "If this leads to the anticipated success"—as predicted by the aminoglycoside art—"it is likely not the product of innovation but of ordinary skill and common sense." *Id.* The claimed "invention" would then be obvious—especially when, as here, no secondary considerations point the other way.

a. The Prior Art Demonstrates That The Claimed "Invention" Is Obvious.

65. The prior art clearly pointed to obviousness. Dosing every 48 hours as claimed in the '689 patent is the product of simple arithmetic. And literally everything pointed towards the '967 patent's once-daily dosing, including the express suggestions by Woodworth and the '226 patent, as further bolstered by daptomycin's known characteristics—concentration-dependent killing, longer half-life, longer post-antibiotic effect, and reversible toxicity. While Dr. Guglielmo attempted to suggest that the art "taught away" from once-daily dosing, his opinions were either withdrawn (*i.e, Baltz* and the *Lee* abstract) or not credible (*i.e.*, the notion that Woodworth "taught away" from the very dosing he recommended).

66. Dr. Guglielmo's opinions are also deficient because he used the wrong legal standard on a core issue, specifically relating to the patent specifications' admission that "aminoglycosides" were "administered as a high dose at less frequent intervals" to "reduce their toxicity." *See supra* ¶ 49; DTX-014, col. 2 ln. 61-65. "Admissions in the specification regarding the prior art are binding on the patentee for purposes of a later inquiry into obviousness." *PharmaStem Therapeutics v. ViaCell*, 491 F.3d 1342, 1362 (Fed. Cir. 2007) (collecting cases). But Dr. Guglielmo did *not* treat the specification as binding:

> Q. In forming your opinion in this case, were you advised that when the specification tells a POSA something about the prior art that that becomes a binding statement for obviousness, for an obviousness analysis? Was that something you were told?
>
> A. I was not told that specifically.
>
> Q. And, in fact, in forming your opinion in this case, you did not treat that statement as binding, did you?
>
> A. I did not. (Tr. 1081:14-22.)

Thus, the Court must disregard Dr. Guglielmo's opinion, because an admissible expert opinion "cannot be based on an erroneous legal premise." *Martinez v. Porta*, 601 F. Supp.2d 865, 866

(N.D. Tex. 2009); *see also Malletier v. Dooney & Bourke*, 525 F. Supp.2d 558, 663 (S.D.N.Y. 2007) (an expert opinion that "is at odds with the substantive law" "must be excluded").

b. Cubist's Evidence Of Secondary Considerations Is Irrelevant, And Does Not Show Nonobviousness In Any Event.

67. Given the state of the art, Cubist spent the majority of its trial time emphasizing secondary considerations: failure of others, long-felt need, and commercial success. But Cubist's evidence, most of which is legally irrelevant, cannot remotely avoid an obviousness finding.

i. Cubist Offered No Proper Evidence Of Either The Failure Of Others Or Long Felt Need.

68. Cubist's main focus at trial was Lilly's decision to "shelve" the dapotomycin project in 1992. According to Cubist, this decision demonstrated the "failure of others" and helped support a "long-felt need." This is perhaps the best example of what Hospira highlighted at the outset of this brief: Cubist's reliance on an analysis that lacks intellectual rigor.

69. Cubist emphasized an alleged "failure" and "need" to treat a specific infection—SAE. But the claims broadly cover treatment of *any* bacterial infection, including skin infections and bacteremia. Lilly proved daptomycin was both safe and effective in treating those conditions. Tr. 590:14-18, 593:17-22, 595:3-597:3 (Zeckel); 664:15-21 (Eisenstein); *accord* DTX-339 Abstract 885 (Lee 1991). This is fatal to Cubist's case.

70. Evidence of secondary considerations "must be commensurate in scope with the claims which the evidence is offered to support." *Rexam*, 731 F.3d at 1264-65. Cubist insists that this view would "wipe out about a hundred years of law." Tr. 1103:14-15. But it is settled that secondary considerations that are "not commensurate with the claim scope" are irrelevant; the "name of the game is the claim." *In re Hiniker Co.*, 150 F.3d 1362, 1369 (Fed. Cir. 1998).

71. Just last year in *Rexam*, for example, the Federal Circuit vacated a grant of summary judgment where the trial court ignored the scope of the claims in analyzing "commercial

success" and "long-felt need." 731 F.3d at 1264. The "central problem," the Court held, was that "the secondary considerations of nonobviousness involved only fragrance-specific uses," like perfumes, "but the claims" were broader—they were "not fragrance-specific." *Id.*

72. Cubist's evidence has the same defect. There was neither a "failure" nor "long felt need" for developing a dosing regimen to treat bacterial infections, including skin infections and bacteremia. If there was any "failure" or "need" at all, it was only to treat SAE, which makes up "something less than five percent" of the market. Tr. 1058:12-15 (Guglielmo).

73. In short, Cubist's evidence of an alleged "failure" and "long-felt need" represents only a tiny slice of the claim scope. Thus, even if the Court accepted Cubist's theory—that Lilly abandoned the project *solely* because it could not find a proper SAE dose—the argument might be relevant to showing nonobviousness of a claim narrowly limited to treating SAE.

74. But Cubist's claims broadly cover indications like skin infections and bacteremia, where Lilly was *successful* years prior. So even if Cubist's narrow "failure" evidence proved that the SAE treatment was non-obvious – which it does not – Cubist's broad claims would *still* be invalid, because claims "broad enough to read on obvious subject matter are unpatentable even though they also read on nonobvious subject matter." *Muniauction, Inc. v. Thomson Corp.*, 532 F.3d 1318, 1328 n.4 (Fed. Cir. 2008).

75. Cubist's failure to provide evidence commensurate with the claim scope is doubly confirmed by two key facts. *First*, Cubicin was on the market for *three year*s without an SAE indication, meaning it was approved to treat nothing more than what Lilly had developed in the early 1990's. Tr. 606:6-11; 680:22-681:1. *Second*, to this day, one of the two asserted dosage amounts—4 mg/kg under claims 16 and 34—is not approved for SAE. Tr. 1058:23-1059:4 (Guglielmo). In other words, this entire argument—which occupied a huge portion of Cubist's

trial time—is irrelevant to two of the four asserted claims of the dosing patents.

ii. Cubist Has Not Shown A Failure Of Others Or Long-Felt Need In Any Event.

76. Even if Cubist's evidence were legally relevant, the evidence still fails as a *factual* matter. Cubist's theme is that Lilly gave up *solely* for technical reasons—because it could not find the right dose to treat SAE. Not so. Cubist's own witness—who was at Lilly in the early 1990s—admitted "that Lilly's decision to terminate the studies wasn't made just on the toxicity issue but it was also in part based on economic considerations." Tr. 667:19-23 (Eisenstein).

77. Economics played a huge role in Lilly's thinking. When developing daptomycin in the early 1990s, Lilly was already selling vancomycin—the gold standard for antibacterials. Tr. 667:24-668:6 (Eisenstein). Vancomycin remains the gold standard today, with 70 percent market share. Tr. 1106:10-13 (Murray). With vancomycin in hand, Lilly set an impossibly high economic bar for daptomycin—one that Cubist itself never cleared. As Dr. Zeckel noted, Lilly would settle only for being the market leader. It "wanted to develop an antibiotic that would be superior to vancomycin if possible and safer than vancomycin, if possible." Tr. 569:19-22.

78. In fact, unlike every other company in the world, Lilly had little incentive to develop daptomycin unless it had "clear advantages over vancomycin." DTX-183 at 1. Unless it was superior, daptomycin would provide Lilly with a net economic benefit of about zero. Tr. 1147:18-21; 1148:19-23. As Dr. Rausser explained, this gave Lilly "very little incentive to cannibalize those sales [of vancomycin] by the introduction of a substitutable drug." Tr. 1147:24-1148:8. Every sale of daptomycin would mean one less sale of vancomycin. *See id.*

79. Lilly thus faced economic incentives not shared by POSAs at other companies, which means its decision does not reflect how other POSAs would have proceeded. This is clear from Lilly's decision. After several successful studies, Lilly encountered—in studies *not* report-

ed in the prior art—two patients with significant CPK elevations and mild symptoms of skeletal muscle toxicity when receiving a daily dose of 8 mg/kg per day (4 mg/kg every 12 hours). Tr. 583:10-11 (Zeckel: "The symptoms were relatively mild.").

80. But it was far from clear that this was a serious problem: 8 mg/kg was at least 33% higher than the now-approved dose (an increased dose can increase toxicity) and it was delivered twice a day in a divided dose (a shorter interval also can increase toxicity). And these mild symptoms occurred in only *two* patients, who both fully recovered. Tr. 598:16-23 (Zeckel). At lower doses with over 100 patients (*see* DTX-339 Abstract 885, DTX-399 Abstract 932), Lilly was unconcerned about skeletal muscle toxicity or CPK elevations. Tr. 596:13-21 (Zeckel); 658:14-23 (Eisenstein).

81. Lilly's *scientists* thus understood the "evidence" was "insufficient" to assess "the true potential for significant CPK elevations." DTX-103 at 1 (Committee Minutes). For more information, the Marketing Committee "recommended . . . additional clinical studies." *Id.* One exceedingly obvious study would be once-daily doses of either 4 mg/kg or 6 mg/kg—a lower daily dose than 8 mg/kg with more recovery time while maintaining or even increasing the individual dose to improve killing power—as Woodworth's later article expressly suggested.

82. Yet these studies were never performed, and it is clear why. Lilly believed—correctly—that it could not meet its *business* goal of producing a better drug than vancomycin. A journal article co-authored by Dr. Eisenstein (then at Cubist), *Daptomycin: From the Mountain to the Clinic with Essential Help from Francis Tally*, makes the point. As that article originally stated: "Because the therapeutic window between efficacy and safety was therefore thought to be small, *taken together with the commercial assessment at Lilly at the time that vancomycin was still reasonably able to deal with infections due to MRSA*, it was decided to discontinue dap-

tomycin development . . . ." DTX-111 at 2 (emphasis added). Dr. Eisenstein admitted this statement was and is true. Tr. 677:16-678:2. But the final version—published after a "review" that included "people from legal"—omitted reference to the commercial assessment. Tr. 678:3-12.

83. Now, in support of its view that it was all about toxicity, not money, Cubist cites testimony of current and former Lilly employees, including at least one paid fact witness. But these witnesses are not disinterested. Aside from being paid, Lilly has a huge incentive to protect Cubist's monopoly. Under the terms of the Cubist-Lilly license agreement, Cubist paid Lilly over $1 million worth of Cubist stock as a license fee. DTX-490 at 8. Further, Cubist agreed to pay Lilly an escalating royalty—10% "on the first $60,000 of aggregate annual Net Sales," and topping out at "17.5% on aggregate annual Net Sales in excess of $120,000,000." *Id*. at 8-9.

84. Nor is there any merit to Cubist's contention that possible "resistance" to vancomycin (VRSA) created a "long-felt need." There was no such need as of the filing date, because the first report of VRSA was in 2002. Tr. 1139:13-17 (Rausser). And in the early 1990s, many thought VRSA "might never" occur. Tr. 669:10-13. The argument also is not commensurate with claim scope, because Lilly successfully developed vancomycin alternatives for most infections by 1992.

85. Cubist makes two additional "long-felt need" arguments. *First*, Cubist contends that drug resistance is allegedly inevitable, so there is always a need for new antibiotics. But this argument proves too much. It would effectively create a long-felt need in *every* antibiotic patent case. Under the law, any such *potential* need is legally insufficient. *Nickola v. Peterson*, 410 F. Supp. 590, 596 (E.D. Mich. 1976) (an "anticipated need" is not a "long felt" need); 60 Am. Jur. 2d Patents § 170 (same). *Second*, Cubist suggests that vancomycin-resistant enterococci (VRE),

which first appeared in 1989, created a long-felt need. But if that was so, Cubicin did not even address that need—the drug is not indicated for VRE. Tr. 1164:3-6 (Rausser).

iii. There Is No Proper Evidence Of Commercial Success.

86. Whatever commercial success Cubist enjoyed, it does not show that once-daily dosing was nonobvious. For Cubist's "objective evidence" to carry "substantial weight," it had to prove "a nexus between the evidence and the merits of the claimed invention." *Ohio Willow Wood Co. v. Alps South, LLC,* 735 F.3d 1333, 1344 (Fed. Cir. 2013). But Cubist did not do so.

87. To the contrary, Stuart Murray, Cubist's 30(b)(6) witness on sales, identified ten attributes of Cubicin that drive sales. Tr. 1106:14-1108:10. Only one—once-daily dosing—relates to the claimed dosing inventions. And as Murray admitted, Cubist has not "formed any conclusions regarding whether any of these attributes caused sales." Tr. 1108:11-14. He was "not aware" of "quantitative analysis" of the issue. Tr. 1108:25-1109:3. Dr. Rausser confirmed the obvious: Cubicin's sales were driven by factors having nothing do with once-daily dosing, such as the inherent bacteria-killing power of the daptomycin molecule. Tr. 1127:3-12; 1132:22-1135:11; *see* DTX-208 at 2, DTX-211 at 2 (analyst reports); *see Aventis Pharma. v. Hospira, Inc.*, 743 F.Supp.2d 305, 348 (D. Del 2010) (Sleet, J.) (finding no nexus absent "evidence that the commercial success of Taxotere is due to anything besides its (prior art) active ingredient").

88. In fact, the evidence affirmatively shows that the convenience of once-daily dosing does not drive sales. Vancomycin is dosed multiple times daily (Tr. 1132:22-1133:12), but it enjoys a market share "in the 70 percent range." Tr. 1106:10-13. Clearly, the "inconvenience" of multiple dosing has not impeded its dominance.

89. Cubist also says once-daily dosing gave Cubist "access" to the market, based on the alleged importance of once-daily dosing to successfully treat SAE. That theory fails for multiple independent reasons. *First,* no court has ever adopted any such "market access" theory.

The law asks what drives sales, and here it is clearly not once-daily dosing. Tr. 1132:22-1135:11 (Rausser). *Second,* Cubist marketed daptoymcin for a full three years *without* the SAE indication, gaining "access" to the market in 2003 using the same indication Lilly had used a decade earlier—skin infections. Tr. 665:1-666:3 (Eisenstein). *Third,* the argument does not even apply to claims 16 and 34, directed to 4 mg/kg dosing, which *to this day* is not indicated for SAE.

III. THE '071 PATENT IS NOT INFRINGED OR, ALTERNATIVELY, INVALID.

A. The CoC Is Invalid, And The Uncorrected '071 Patent Is Not Infringed.

1. Proposed Findings Of Fact

a. The Importance Of Stereochemistry

90. Daptomycin's tail contains an amino acid called asparagine. As Hospira's expert, Dr. Ganem, testified, a POSA before 2001 would have had no reason to doubt that asparagine had the "L" stereochemical configuration (L-Asn). Tr. 133:13-17.

91. Stereochemistry can be critically important. It "is not unusual" for "stereoisomers" to have "significantly different properties." Tr. 143:7-9 (Ganem); DDX-Ganem-029 (Vitamin C). Accordingly, the FDA has dictated that stereoisomers "are both commercially distinct and pharmacologically different and therefore should be treated as separate drugs and developed accordingly." Tr. 143:10-144:4 (Ganem explaining FDA's guidance); DTX-259.

92. Here, for instance, both experts agreed that D-Asn daptomycin and L-Asn daptomycin have different properties (Tr. 150:4-15 (Ganem); 828:5-11 (Gerwick)), and that D-Asn daptomycin is ten times more potent. Tr. 140:5-141:2 (Ganem); 828:12-16 (Gerwick).

b. As Of 1987, Scientists Could Make Daptomycin Either Through Fermentation Or Semi-Synthetically.

93. The experts agreed that scientists have made antibiotics semi-synthetically since the 1960s. Tr. 131:7-19 (Ganem); 842:12-18 (Gerwick). At trial, Cubist nevertheless highlight-

ed the '071 patent's references to using natural fermentation instead. But contrary to Cubist's *Markman* position, it is now undisputed that in 1987 (the priority date), daptomycin could be made by either natural fermentation or chemical synthesis. Tr. 841:6-16 (Gerwick); 122:16-124:5 (Ganem describing '717 patent); 130:12-131:6 (Ganem describing Debono 1988). Dr. Gerwick candidly admitted that scientists could make "semi-synthetic versions of both D and L" using a "standard" method available "since the late 1980s." Tr. 841:17-842:18.

94. Further, contrary to another position that Cubist took at *Markman*, a POSA had the tools in 1987 to determine the correct stereochemistry of daptomycin. Indeed, as Cubist admitted in *Cubist v. Teva*: "[I]t would have been possible to determine which amino acid had been mischaracterized using technology available in the 1980s." Cubist Findings of Fact, No. 1:09-cv-0189, Dkt. 126-1 at 243 (D. Del. Mar. 4, 2011).

95. Dr. Ganem identified two specific methods that were then known in the art. Tr. 128:6-11. *First*, a POSA could have broken the molecule into individual amino acids and compared each amino acid's optical activity to a known standard. Tr. 128:12-21. In fact, the inventors tried to do this, but in "otherwise beautiful" work, they mistakenly used different solvents for the test and the standard, producing an incorrect result. Tr. 128:22-129:6. Absent that basic error, they would have correctly determined daptomycin's stereochemistry—in 1987. *Id.*

96. *Second*, a POSA could have used a reaction called the "Edmond Degradation," which was discovered in the 1950s and has been in chemistry textbooks since the 1960s. Tr. 129:14-17. Under this procedure, a POSA would have easily confirmed the correct stereochemistry by detaching the asparagine, re-attaching it in two different ways, and comparing the results. Tr. 129:7-130:6. The inventors never conducted this basic work.

c. Cubist Determined The Correct Stereochemistry In 2001, But Waited For Six Years—Until 2007—Before Telling The Patent Examiner Of The '071 Patent.

97. As early as 2001, Cubist knew that the substance previously referred to as "daptomycin" was actually D-Asn, not L-Asn. DTX-006 (disclosing that provisional application was filed in 2001); Tr. 135:11-136:19 (Ganem explaining DTX-006).

98. Cubist did not seek peer review of its findings until 2005, when an article by Cubist's Vivian Miao revealed that daptomycin was D-Asn rather than L-Asn. Tr. 137:24-138:8 (Ganem); DTX-359 (Miao 2005). To make this determination, Miao performed a "straightforward experiment." Tr. 141:2 (Ganem). She used the prior art Edmond Degradation method to detach two amino acids, used peptide synthesis to make two different stereoisomers, and then compared their properties. Tr. 140:5-141:14 (Ganem). As Dr. Ganem observed, "all of this would have been possible in 1987." Tr. 141:15-21. Dr. Gerwick agreed. Tr. 841:17-842:18.

99. Yet the patent examiner on the '071 patent had to wait two more years to learn the truth. Not until late 2007, well after the '071 patent issued, did Cubist supply the patent office with the Miao article. Tim Douros, Cubist's in-house counsel, admitted he was aware of this discovery *before* the '071 patent originally issued, but had no explanation for why it was never raised with the patent office until *after* patent issuance. Tr. 202:11-21.

d. Cubist Sought A CoC, And Has Repeatedly Relied On The Wrong Legal Standard.

100. In connection with its belated disclosure of the Miao article, Cubist sought a Certificate of Correction ("CoC") to change the chemical structure of daptomycin (called "Formula 3" in the claims) from L-Asn to D-Asn. Cubist's submission was cursory. It recited the relevant statutory text—a mistake of "minor character"—but never explained why its proposed correction would not be "broadening" under the controlling legal standard. Indeed, a CoC is invalid if the

corrected claim "contains within its scope any conceivable apparatus or process which would not have infringed the original patent." *Tillotson, Ltd. v. Walbro Corp.*, 831 F.2d 1033, 1037 n.2 (Fed. Cir. 1987). Cubist never mentioned that standard. PTX-008 at CUBH 000437-438.

101. Cubist makes much of the fact that its lawyers called the patent office to "determine whether a certificate of correction was appropriate." Tr. 838:11-20; PTX-008 at CUBH 000438. But as Dr. Gerwick admitted, there is no record of this conversation. Tr. 838:24-839:10. And even if there were, it could not change the governing standard.

102. It is easy to see how the examiner may have been led astray. To obtain a CoC, Cubist had to show *both* that the mistake was "of minor character" *and* that the correction did not "involve such changes in the patent as would constitute new matter or require re-examination." 35 U.S.C. §255; Manual of Patent Examining Procedure §1481. This case turns on the first requirement, which Cubist indisputably cannot meet. But before this Court, Cubist has repeatedly stressed the second one, which, while perhaps more debatable, is currently irrelevant. *E.g.*, D.I. 48 at 9-10 & n.11; D.I. 51 at 17:24-25 (referencing a "body of law built around this concept of new matter"); D.I. 110-9 at 94-95 (¶¶ 268-69). It is no leap to conclude that Cubist may have similarly encouraged the examiner to focus solely on the wrong requirement.

e. Cubist's Own Conduct Demonstrates It Knows The CoC Broadened The Claims.

103. Regardless, Cubist's own *actions* before the FDA confirm that it knows the CoC is invalid. Specifically, Cubist delisted the patent from the Orange Book *before* the correction (conceding the patent did *not* cover D-Asn daptomycin) and relisted the patent *afterwards* (contending the corrected patent *does* cover D-Asn daptomycin).

104. Under FDA regulations, "[a]n applicant [for an NDA] shall submit the required information … for each patent that claims the drug … and with respect to which a claim of pa-

tent infringement could reasonably be asserted" against an ANDA filer. 21 C.F.R. § 314.53(b)(1). Although initially listing the '071 patent in the Orange Book in 2006, Cubist *delisted* the patent a year later in 2007. Tr. 203:3-17. As Mr. Douros testified, the delisting decision was purely legal—only lawyers were involved. Tr. 205:16-18; Tr. 205:3-8, 13-15. In fact, Cubist's current trial counsel at Wilmer Hale first recognized that the '071 patent needed to be delisted. Tr. 205:19-206:2. And there was only one possible reason to delist: the '071 patent *did not cover the drug*, which necessarily means the CoC is invalid.

2. Proposed Conclusions Of Law On CoC Invalidity

105. A CoC may be used to correct only two kinds of mistakes—either "a mistake of a clerical or typographical nature, or of minor character." 35 U.S.C. § 255. Mr. Douros admitted that the mistaken stereochemistry was not a mistake of a "clerical or typographical nature." Tr. 202:22-203:2. Thus, the only issue is whether the disputed "mistake" was "of minor character."

106. "[A] mistake the correction of which broadens a claim is not a 'mistake of … minor character.'" *Superior Fireplace Co. v. Majestic Prods. Co.*, 270 F.3d 1358, 1376 (Fed. Cir. 2001). And determining whether a claim is "broadened through correction requires interpreting the old and new versions of that claim, and then determining whether the new version covers territory the old one did not." *Central Admixture*, 482 F.3d at 1353. Indeed, a CoC is invalid if the corrected claim "contains within its scope *any conceivable apparatus or process* which would not have infringed the original patent." *Tillotson*, 831 F.2d at 1037 n.2 (emphasis added). Finally, a product is covered by a claim only when it satisfies "each and every element" of the claim. *Aristocrat Techs. Australia Pty Ltd. v. Int'l Game Tech.*, 709 F.3d 1348, 1363 (Fed. Cir. 2013).

107. The CoC here plainly broadens the claims, which are directed to, among other elements, "a compound of Formula 3." DTX-001, claims 18, 26. As Dr. Gerwick admitted, daptomycin with D-Asn was not covered by "Formula 3" before the correction—only after:

Q. So D-Asn is not covered before the correction with respect to Formula 3 itself. Right?

A. Formula 3 with D-Asn is different than Formula 3 with L-Asn. That is self-evident, yes.

* * *

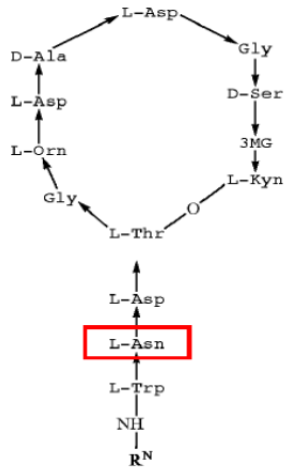
Q. Then after the correction, D-Asn would be covered by Formula 3. Correct?

A. Formula 3 as corrected would cover D-Asn, as would the fermentation product also cover D-Asn. Tr. 837:20-838:6; *accord* 149:5-21.

108. To attempt to escape the consequences of these "broadening" admissions, Cubist simply ignored the controlling legal standards. *First*, Dr. Gerwick admitted that when offering his opinion on direct, he never applied the governing broadening standard: "We didn't speak of that, no." Tr. 835:18-21. *Second*, he admitted he did not know how to determine what a claim covers, which requires considering whether a product is "covered by each and every element of the claim." Tr. 837:14-18. When asked if he "applied" that basic "principle" when "developing your opinions," Dr. Gerwick conceded, "No, I did not." Tr. 837:14-18.

109. These deficiencies left Dr. Gerwick's opinion—and Cubist's case—untethered to any relevant authority. He essentially suggested that because the error affected only one of thirteen stereocenters, the error was of minor character. Tr. 824:24-825:7. This has *no relationship whatsoever* to the scope of the claims, and ignores the proper legal standard.

110. Aware of this difficulty, Cubist tries to append a "process limitation" to its claims —a fermentation limitation—arguing that D-Asn daptomycin would have been covered by the revised "fermentation" claim both before and after the correction. *E.g.*, Tr. 814:7-11 (Gerwick) ("the fermentation product has always been the same"). The argument is frivolous.



111. *First*, it ignores the fact that "Formula 3" is a chemical

structure *expressly* set forth in the claims. It is one of the claim elements, depicted on the right before the correction. DTX-001 col. 16, col. 21. In other words, any attempt to artificially add a process limitation cannot change one simple fact: the D-Asn molecule could never satisfy the uncorrected limitation of Formula 3.

112. *Second*, as both experts agreed, the claims do not include a process limitation. Dr. Gerwick admitted this point on cross examination:

> Q. My question, though, is does the claim restrict the scope of the claim to daptomycin made through fermentation?
>
> A. I don't see it expressly stated in the claim.

Tr. 840:15-17. In fact, he flatly admitted that the claim "covers daptomycin with a D molecule made by fermentation or any other means." Tr. 840:21-841:1. And while Dr. Ganem acknowledged that the *specification* referred to daptomycin produced by fermentation, he never deviated from his view that the *claims* did not require "any particular process." Tr. 188:11-19.

113. *Third*, settled law bars adding a process limitation. "As a general proposition, a limitation that does not exist in a claim should not be read into that claim." *Biovail Corp. Int'l v. Andrx Pharm., Inc.*, 239 F.3d 1297, 1301 (Fed. Cir. 2001). And adding a nonexistent process limitation to a *product* claim is particularly inappropriate. "The method of manufacture, even when cited as advantageous, does not of itself convert product claims into claims limited to a particular process." *Vanguard Prods. Corp. v. Parker Hannifin Corp.*, 234 F.3d 1370, 1372-73 (Fed. Cir. 2000). In rare circumstances, courts will add process limitations to product claims, but only when the patentee has excluded all other possible processes through "a clear intention to limit the claim scope using 'words or expressions of manifest exclusion or restriction.'" *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 906 (Fed. Cir. 2004). That did not happen here.

114. Once the CoC falls away, Hospira prevails based on non-infringement. Hospira's

ANDA and 505(b)(2) products are D-Asn daptomycin, which Dr. Gerwick admitted was not covered by the uncorrected patent. Tr. 837:20-838:6.

B. If The CoC Is Valid, The '071 Patent Is Invalid For Lack Of Written Description.

115. Even if the CoC *were* somehow valid, the '071 patent would then be invalid for lack of a written description. To satisfy the written description requirement, the specification "must 'clearly allow persons of ordinary skill in the art to recognize that the inventor invented what is claimed.'" *Ariad Pharms.*, 598 F.3d at 1351 (citation and brackets omitted). As applied here, that means a POSA would have had to recognize that the inventors had the idea for D-Asn daptomycin on the filing date in 1987.

116. Cubist cannot meet this standard. As Dr. Ganem explained, a POSA reading the specification "would only find mention of daptomycin having the L-Asn configuration" and thus "see no evidence" "the inventors were in possession" of the D-Asn molecule. Tr. 151:21-152:9. Dr. Gerwick agreed, admitting the 1987 specification did not "reasonably convey" D-Asn:

> Q. Meaning that the specification, before the correction, did not reasonably convey to one of ordinary skill in the art that these inventors had the idea for Formula 3 with a D-Asn. True?
>
> A. I guess that's true, yes. Tr. 834:19-23; *accord* 831:23-832:3.

117. Cubist alternatively argues that the inventors "physically possessed" D-Asn daptomycin, the fermentation product. But the Federal Circuit rejected that argument in *In re Wallach*, 378 F.3d 1330 (Fed. Cir. 2004), where the patent claimed a protein defined by a partial amino acid sequence. The patentee argued that it met the written description requirement through "possession " of the claimed protein, which it argued "necessarily" meant "possession of its inherent amino acid sequence." *Id*. at 1334. But as the Court explained, "that Appellants may have isolated and thus physically possessed [the claimed protein] does not amount to knowledge

of that protein's sequence or possession of any of its other descriptive properties." *Id.* at 1334-35.

118. So too here: the inventors' possession of D-Asn daptomycin does not amount to knowledge of the *claimed* stereochemical structure depicted by *corrected* Formula 3. Cubist thus loses based on a violation of the written description requirement. And because none of its applications comply with that requirement, Cubist loses the benefit of any of those applications for a priority date, which means the corrected '071 patent also would be invalid for anticipation over the commercial sale of daptomycin in 2003.

C. The '071 Patent Is Invalid Under The Rule Against Improper Recapture.

119. The asserted claims of the '071 patent, a reissue patent, are also invalid for another reason—improper recapture. A patentee may not "regain[] through reissue the subject matter that he surrendered in an effort to obtain allowance of the original claims." *Pannu v. Storz Instruments, Inc.*, 258 F.3d 1366, 1370-71 (Fed. Cir. 2001). That is just what happened here: To obtain its original '226 patent, Eli Lilly "surrendered" subject matter that was later "recaptured" in the asserted claims of the reissued '071 patent.

120. In the original prosecution, Lilly pursued original claim 24, which covered an effective amount of daptomycin, with a suitable vehicle, in "substantially pure form."[8] The specification defined "substantially pure" as daptomycin with less than 2.5 percent of a combined total of two derivatives, later called "Formula 1" and "Formula 2." DTX-002 col. 8 ln. 58-60.

121. The PTO repeatedly rejected claim 24 as obvious over the 1986 Debono patent, which disclosed a compound with a similar peptide structure. DTX-532 at CUBT 0002964. For

[8] The full claim read: "A composition useful for the treatment of susceptible bacterial infections comprising an effective antibacterial amount of the new drug substance LY 146032, or a pharmaceutically-acceptable salt thereof, in substantially pure form, together with a suitable vehicle." DTX-532 at CUBT 0002956-57.

over three years, Lilly insisted that claim 24 was patentably distinct from Debono. But Lilly finally gave up—cancelling claim 24—and the remaining claims were then allowed years later. "[T]he purpose of [Lilly's] amendment [i.e., cancellation] was to overcome the prior art and secure the patent." *MBO Labs., Inc. v. Becton, Dickinson & Co.*, 602 F.3d 1306, 1314 (Fed. Cir. 2010).[9]

122. In reissuance, however, Cubist obtained the two asserted claims (18 and 26) covering the very same subject matter—and then some—as surrendered claim 24. The reissued claims are directed to compositions or pharmaceutical formulations comprising the same compound with less than 6.0%—thus covering less than 2.5%—of the same two derivatives, "Formula 1" and "Formula 2." DTX-001 claim 18, 26. That is a textbook case of improper recapture.

123. Hoping to avoid invalidity, Cubist says asserted claim 26 is "narrower" than surrendered claim 24 because, for example, it is directed to a "pharmaceutical formulation." *See Pannu*, 258 F.3d at 1371 (requiring that the court determine "whether the reissued claims were materially narrowed in other respects to avoid the recapture rule"). But this just means the active ingredient is combined with something else so it can be administered to a patient—the same concept reflected in canceled claim 24's requirement of a "suitable vehicle." Cubist also says claim 26 "limits" Formula 3 to "about 0.1 to about 90 weight percent" of the pharmaceutical formulation. But this is so broad that it does not narrow at all, much less materially.

124. Finally, Cubist argues (incorrectly) that the asserted claims require the two impurities to be present, while the surrendered claim did not. Even if it were true that the asserted claims require the presence of "Formula 1" and "Formula 2," there still would be no *material*

[9] Cubist says claim 24 was cancelled in response to a §112 rejection, but it was *also* rejected for obviousness. And Lilly had argued for *3.5 years* that claim 24 was patentably distinct from the prior art. *See, e.g.*, DTX-532 at CUBT0002975 (11/4/88 Response), CUBT0002988 (8/25/89 Response). A reasonable observer could only conclude Lilly gave up.

narrowing. The original claim was directed to substantially pure daptomycin (Formula 3), and it is not materially altered simply by requiring that "Formula 1" and "Formula 2" be present in a non-zero amount less than 6%.

125. In sum, after Lilly surrendered claim 24 to avoid obviousness, Cubist recaptured the same subject matter through reissuance of the asserted claims, rendering them invalid.

IV. THE PURITY PATENTS ARE INVALID.

126. The asserted claims of the purity patents are likewise invalid as a matter of law. Each asserted claim—claims 91, 98, and 187 of the '238 patent, and claims 23 and 53 of the '342 patent—is a product-by-process claim (or a method of making a composition containing a product-by-process), and they all claim purity levels ranging from 93% to 97% as measured against 14 specified impurities. DTX-003 ('238 patent); DTX-008 ('342 patent).

127. As outlined below, (1) the asserted claims are grossly invalid under the "general rule" for product-by-process claims, which ignores process limitations for a validity analysis; (2) Cubist cannot avoid that rule through a rare functional/structural exception; and (3) even if the exception applied, the asserted claims would remain invalid.

A. Proposed Findings Of Fact

1. Purification Is Routine.

128. By 2000, the priority date, purification was routine and, indeed, partly automated. Tr. 399:9-16; 404:5-10; 407:19-22 (Baker). Standard textbooks, such as *Protein Purification*—written for undergraduates and beginners (Tr. 405:12-406:5)—taught that "complete purification" could "normally be done in a short period of time." DTX-385 at 16. Dr. Baker explained it typically takes "one or two weeks." Tr. 403:8-11.

129. Because purification is so "routine" and "not really considered to be that interesting" (Tr. 399:14-16), Dr. Baker has conducted and taught basic purification extensively for near-

ly 30 years (Tr. 397:21-24) without ever publishing an article on the topic. Tr. 399:9-12. And although his company has purified approximately 5,000 compounds since its inception, it has never sought a patent on the purification of a fermentation product. Tr. 404:1-10. Though Dr. Gerwick has 20 patents, and has purified 100-150 lipopeptides such as daptomycin, he has no patents on any purification technique used to purify a lipopeptide. Tr. 868:9-869:13.

130. Mr. Paul Lynch, an inventor on the purity patents, also confirmed that purification was routine. His company performs purification services for a fee, and applies a "standard set of steps" to identify a useful process for purifying any particular molecule. Tr. 430:13-431:18. He applied this "standard" approach during his eight years with the company for "prior clients." Tr. 433:3-11. But other than Cubist, no client has ever listed him as inventor on a patent for purifying *any* molecule other than daptomycin. Tr. 433:3-434:9.

2. Purifying Daptomycin Was Routine.

131. Lilly's prior art '843 patent reported daptomycin purity of 93% (DTX-012 col. 2 ln. 40-44), only four percent below the highest level (97%) required by Cubist's asserted claims. And it required mere routine work to increase daptomycin's purity another six percent to over 99%.

132. Cubist hired Mr. Lynch to perform this work, asking him to use his "standard approach" to "purifying daptomycin." Tr. 431:19-432:4. Based on that approach, Mr. Lynch identified the pH range, salt, temperature, and loading to optimize the conditions for purifying daptomycin. Tr. 432:5-17. And he did this by applying "the same general types of testing as [he] would have performed in the ordinary course to determine the type of resins and the process conditions for purifying other molecules." Tr. 433:16-21. The ultimate purification conditions are unique to each molecule, but Mr. Lynch's job was to determine those conditions by a standard process. As he put it: "That's what we do[.]" Tr. 434:3-9.

133. Without identifying what specific step of Mr. Lynch's process was supposedly inventive, Cubist now says this "standard approach" was patentable. But Mr. Lynch has done the same thing countless times. And in the case of daptomycin, Dr. Baker confirmed that none of the conditions Mr. Lynch allegedly "discovered" were new or remarkable. Tr. 440:16-441:13.

134. Example 2 of the purity patents describes the results of this standard process. As Dr. Baker explained, "[t]hey took material that had been prepared by a method disclosed by previous patents, and then passed the material over an ion exchange column." Tr. 437:18-22. Specifically, Mr. Lynch started with daptomycin purified according to the method taught in Lilly's prior art '843 patent, which discloses a process that "improves the purity of [daptomycin] two-fold and … improves the final purity from about 80 percent to about 93 percent." DTX-012 col. 2 ln. 40-44; Tr. 414:13-22. Then, Mr. Lynch passed this daptomycin over an ion exchange column – just one time—to produce daptomycin greater than 99% pure. Tr. 439:9-19.

135. This was nothing new. The *Protein Purification* textbook—again, aimed at undergraduates and beginners—taught students to begin their purification efforts with ion exchange chromatography. Tr. 434:22-436:2. Ion exchange is an old process, first developed in 1959. Tr. 407:10-16. In Dr. Baker's words, this process was an "obvious candidate[]." Tr. 435:22-436:2. Indeed, he had "never" worked in a laboratory that did protein purification that did not have an ion exchange column, and had never set foot in such a laboratory. Tr. 436:3-8.

136. Despite Cubist's effort at misdirection during Dr. Gerwick's direct examination, nothing in the '843 patent "taught away" from using an ion exchange column to increase purity. This traditional tool had one problem: It was less effective when the material had a high saponin content, because that impurity can "clog[] up the works." Tr. 873:20-874:9 (Gerwick). But the entire point of the '843 patent was to solve that problem. Tr. 874:10-12 (Gerwick). And it did:

The claimed "reverse method purification" produced daptomycin of 93% purity without saponins. Tr. 875:6-13. Dr. Gerwick conceded the patent is "silent about any other steps they take after that." Tr. 875:14-16; *accord* 414:23-415:2 (Baker). Once the saponins were removed, a POSA would have known that ion exchange was perfect for increasing daptomycin's purity above 93%. *Supra* ¶ 135.

3. Cubist's Product Is Not Structurally Or Functionally Different From The Prior Art.

137. Cubist mainly tried to defend the purity patents with the rare functional/structural exception. But that exception requires both a structural *and* a functional difference. Yet Cubist never even tried to show a functional difference. There is none. Barry Eisenstein, who was in charge of Lilly's daptomycin trials, admitted that Lilly administered daptomycin to over 100 patients with "no toxicities that anybody at Lilly ever saw from patients that were administered batches of daptomycin that were caused by" either "endotoxins" or "saponins." Tr. 661:11-20. Dr. Gerwick admittedly had no basis to say otherwise. Tr. 845:11-846:5, 847:14-16.

138. Nor, for three reasons, are there structural differences between Cubist's product and the prior art. *First*, the removal of saponins does not distinguish Cubist's product from the prior art '843 patent. As Gerwick admitted, the *entire point* of the '843 patent was to remove saponins. Tr. 873:9-874:12. The patent's Example 1 expressly discloses the "remov[al of] non-uv impurities, e.g., the saponins." DTX-012, col. 4 ln. 23-25. And the patent claims a process "to remove non-uv impurities" such as saponins. DTX-012 claim 1(d). No wonder, then, that Lilly had produced 13 daptomycin lots with saponin amounts below the level of detection—a fact Cubist admitted to the FDA. Tr. 853:7-9 (Gerwick); DTX-031 at 74-75.

139. *Second*, as Dr. Gerwick also admitted, "companies have been successfully removing endotoxins from fermentation-produced products for decades." Tr. 858:23-859:1. Lilly was

one such company. Lilly had a "standard" for what constituted a pyrogenic lot, which was even more rigorous than the FDA's USP standard, and Lilly met both standards. DTX-116 (LY146032 Endotoxin Levels); Tr. 475:25-476:22 (Baker); DTX-186 (Daptomycin Final Product Lots). Gerwick agreed that "some of the Lilly lots had sufficiently low endotoxin levels to deliver to human beings." Tr. 857:9-858:1.

140. *Third*, examples from the patents themselves prove that micelle filtration does not increase purity to the point where the resulting daptomycin is somehow "structurally and functionally" different. On the contrary, the micelle filtration examples actually produced substantially *lower* purity than examples using other standard purification methods:

Non-Micelle	**Purity Level**	**Micelle**	**Purity Level**
Example 2	"greater than 99%"	Example 11	"40 to 80% or greater"
Example 5	"approximately 98% to 99%"	Example 13	"85% pure"
Example 6	"greater than 99%"	Example 14	"80-90% pure"
Example 7	"99.0 to 99.5% pure"	Example 15	"approximately 93%"
Example 8	"98.5 to 99.5% pure"	Example 16	"approximately 93%"
Example 10	"greater than . . . 99.0%"		

DDX-Gerwick-011; Tr. 859:22-861:15. Dr. Gerwick admitted he saw no "structural and functional" difference between these two sets of examples. Tr. 865:8-18. In response, Cubist argued that the non-micelle examples were not published prior art. That's irrelevant. The point is that Cubist's allegedly "novel" process step—micelle filtration—clearly does not produce "structurally and functionally" different daptomycin as compared to daptomycin produced using any other conventional purification method, such as example 2's use of an ion exchange column.

4. The Prior Art Taught That Micelle Filtration Could Be Used To Purify Surfactants Like Daptomycin.

141. Even if the claimed process steps were legally relevant, Cubist's asserted claims would still be obvious. As Dr. Baker explained at trial, every single process step in the claims was well known in the prior art; and other than micelle filtration, each process had actually been

applied to daptomycin itself. Tr. 477:19-478:12, DDX-Baker-019 (anion exchange chromatography); 479:1-9, DDX-Baker-020 (hydrophobic interaction chromatography); 479:10-21, DDX-Baker-021 (size exclusion chromatography); 479:22-480:3, DDX-Baker-022 (HPLC).

142. There is no dispute that micelle filtration was a known purification process. A 1997 paper by Lin taught the use of micelle filtration to purify a "surfactant" called "surfactin" and then broadly stated that the process "can be further modified and employed for the recovery and purification of most surfactants." DTX-345 at 416; Tr. 490:16-494:2 (Baker); Tr. 890:13-891:3 (Gerwick). And as Dr. Gerwick conceded, daptomycin is a surfactant. Tr. 890:22-24.

143. To attempt to avoid obviousness, Dr. Gerwick argued that it was not yet "known" daptomycin was a surfactant before Cubist's "invention." Not so. As Dr. Baker explained, a POSA would have known daptomycin was a surfactant based on two key points:

- ***Concentration-dependent aggregation***. As the 1988 Lakey article explains, "aggregation [of daptomycin] occurs at concentrations higher than 10 to the minus 3 molar." Tr. 485:6-24; *see* DTX-333 at 4643. Concentration-dependent aggregation is an intrinsic property of surfactants. Tr. 485:10-24.
- ***Movement toward the lipid-water interface***. As the same Lakey article explains, daptomycin moves to the lipid-water interface. DTX-333 at 4643; Tr. 485:25-486:4. This is how surfactants behave. Tr. 481:9-16; 486:22-487:1.

144. Dr. Gerwick had no rebuttal. He could only *disagree* with the Lakey article's teaching about concentration-dependent aggregation. Tr. 804:18-20 ("I don't fully concur with their interpretation"). But the article teaches what it teaches. And Dr. Gerwick did not even address the article's teaching on phase interaction.

145. It is true that whether a given molecule will actually form micelles depends on temperature, pH, and salt concentration. Tr. 483:22-484:1. But as Dr. Baker explained, it would only take "[a]n afternoon" to "catalog the conditions that produce micelles for any particular molecule." Tr. 484:16-19. This is the definition of routine experimentation.

146. In sum, a POSA would have known (1) that daptomycin formed micelles, (2) how to purify with micelle filtration, and (3) how to apply micelle filtration to daptomycin.

B. Proposed Conclusions Of Law

1. The Prior Art Demonstrates That The Claims Are Obvious And, In One Case, Anticipated.

147. All of this confirms that the clamed "invention" is simply a product "of ordinary skill and common sense," which makes it exceedingly obvious. *KSR*, 550 U.S. at 421. When "determining validity of a product-by-process claim, the focus is on the product and not the process of making it." *Greenliant Sys., Inc. v. Xicor LLC*, 692 F.3d 1261, 1268 (Fed. Cir. 2012). Under this "general rule," the process limitations are "irrelevant." *Id.*

148. There is no basis to uphold the asserted claims under the "general rule." It is not an invention to use a decades-old and highly popular purification column—just once—to improve the purity of prior material from 93% to over 97%. As Dr. Baker stated, a scientist unconcerned about yield—and the claims have no yield requirements—could easily achieve even higher purity simply by running material over a variety of different columns (losing some material each time but easily achieving near perfect purity), as taught in basic textbooks. Tr. 451:2-20.

149. Claim 98 of the '243 patent, directed to 93% purity, is not only obvious but anticipated. During prosecution, Cubist admitted that the "'843 patent describes that . . . the highest yields obtained were about 93%, i.e., 93% daptomycin versus the fourteen daptomycin impurities[.]" DTX-246 at 14, Tr. 446:3-12 (Baker); DDX-Baker-012. As Baker explained, there is no difference between the two, so claim 98 is anticipated. Tr. 445:20-446:2; 447:1-10. Dr. Gerwick admitted all of this: "I cannot identify a difference at this moment." Tr. 888:20-24.

150. In its main attempt to save the purity patents, Cubist tries to avoid the general rule based on an exception that the Federal Circuit has applied just *once* in 25 years. *Amgen Inc. v. F.*

Hoffmann–La Roche Ltd., 580 F.3d 1340, 1369 (Fed. Cir. 2009). In *Amgen*, the prior art disclosed a natural-source molecule (EPO, a protein), while the asserted patent claimed EPO "purified from mammalian cells grown in culture." *Id.* at 1367. As the court held, the patent would be valid only if "the production of EPO by recombinant technology resulted in a new product." *Id.* It did—recombinant EPO had "a higher molecular weight and different charge … due to differences in carbohydrate composition." *Id.* Thus, recombinant EPO was *necessarily and always* a different molecule from natural EPO, and it behaved differently. *Id.* at 1365.

151. This case is nothing like *Amgen*. Cubist asserts that micelle filtration produces a structurally and functionally "new" composition based on the alleged elimination of saponins and endotoxins or a different impurity profile. But as Dr. Gerwick admitted, "nothing in the claims … says saponin-free." Tr. 847:21-23; *accord* Tr. 847:17-20. In fact, the purity patents do not even *mention* saponins (Tr. 847:24-848:6), and no asserted claim refers to removing endotoxins (Tr. 853:23-854:13). Yet other, non-asserted claims *do* mention "depyrogenating daptomycin"—the removal of pyrogens (endotoxins)—confirming that the inventors knew how to include that limitation. *See, e.g.*, DTX-003, claim 77; *see also* DDX-Gerwick-010 (claim comparison).

152. Moreover, Dr. Gerwick agreed that, as far as he knew, he was "the first person to argue that saponin and endotoxin levels are what justify the validity of these patents." Tr. 843:17-20. Not once during the decade-long prosecution of the purity patents did anyone argue that Cubist's invention was different from the prior art based on saponin and endotoxin levels. Tr. 844:10-22.

153. And for good reason: Any purported "functional" difference is flatly refuted by the successful administration of Lilly's prior art material to over 100 patients. And any purported "structural" differences are flatly refuted *at least* by the patent examples (showing consistent-

ly greater purity with non-micelle purification), Lilly's prior art lots (many of which were saponin- and endotoxin-free), and the fact that companies have been removing endotoxins from fermentation products for literally decades.

154. Even if the Court applied the structural/function exception, the claims would *still* be invalid. Micelle filtration was obvious because the Lin article taught micelle filtration for "purification of *most surfactants*" (Tr. 890:13-23 (emphasis added)), and Dr. Gerwick offered no credible answer to Dr. Baker's opinion that daptomycin was a known surfactant, which, in any event, could have been tested in an "afternoon." Tr. 484:16-19.

2. Secondary Considerations Demonstrate That The Purity Patents Are Obvious

a. There Is No Nexus Between The Purity Patents And Any Secondary Consideration Relied On By Cubist.

155. Cubist did not even try to link any secondary consideration to the "inventions" claimed in the purity patents. On the contrary, for commercial success, Cubist's Mr. Murray testified that purity "typically has no bearing on whether or not a physician will prescribe a drug." Tr. 1109:4-9. Undeterred, Cubist says the purity patents met a long-felt need for manufacturing highly pure daptomycin "on a commercial scale at a yield that would make a commercial process viable." Tr. 915:20-916:5. The problem is, the claims make no mention of yield or commercial scale. Tr. 930:13-931:9 (Myerson); Tr. 744:3-15 (Kelleher). The claims thus cover even bench-top purification with exceedingly low yields.

b. Lilly's Simultaneous Invention Demonstrates That The Purity Patents Are Obvious.

156. Another secondary consideration, invention by another, further supports a finding of obviousness. "Independently made, simultaneous inventions … are persuasive evidence that the claimed apparatus 'was the product only of ordinary mechanical or engineering skill.'" *Geo.*

M. Martin Co. v. Alliance Machine Sys. Int'l, 618 F.3d 1294, 1305 (Fed. Cir. 2010) (citation omitted). Here, as Cubist admitted to the FDA, Lilly manufactured 98% pure daptomycin not just simultaneously, but a decade before Cubist did. DTX-079 at 124; Tr. 417:17-418:19; 727:24-728:13; 883:21-884:12.

3. The Purity Patents Are Invalid Under § 102(f).

157. The purity patents are invalid for yet another reason under 35 U.S.C. § 102(f), which applies when (1) there is prior conception of the invention by another, and (2) communication of that conception to the patentee. *Oleksy v. General Electric Co.*, No. 06 C 01245, 2013 WL 3233259, at *19 (N.D. Ill. Jun. 26, 2013). That is what happened here.

158. The first party to invent highly pure daptomycin was Lilly. As noted, in the case of product-by-process claims, the "invention" is the final product—highly pure daptomycin. That Cubist used another way to make it—the process steps—is irrelevant.

159. Cubist essentially admitted invalidity under §102(f) to the FDA, acknowledging that Lilly obtained 98% pure daptomycin *over a decade before Cubist's priority date*. *See* ¶ 156. And Lilly communicated that patent-defeating work to Cubist. As Kelleher stated, Cubist's "invention was to … build upon a foundation that Lilly had laid." Tr. 721:11-24. He could not deny that under the Lilly-Cubist license agreement, Lilly provided Cubist with batch records, actual batches, yield data, and clinical data. Tr. 719:5-23. In short, Lilly gave Cubist its invention and permission to take it to market—but not to patent it. Thus, the asserted claims violate §102(f).

V. THE PURITY AND DOSING PATENTS ARE EITHER INVALID FOR A LACK OF WRITTEN DESCRIPTION OR NOT INFRINGED.

160. As with the '071 patent, Cubist faces an intractable dilemma for the dosing and purity patents: The asserted claims are either invalid for a lack of written description or not infringed under the correct claim construction.

A. The Purity And Dosing Patents Are Invalid Due To Lack Of Written Description.

161. For the purity and dosing patents, this Court has construed the claim term "daptomycin" to mean D-Asn daptomycin, based on the addition of a process limitation that inherently excludes L-Asn and includes D-Asn—specifically, an "antibiotic derived from the fermentation of Streptomyces roseoporus." D.I. 59 at 1. But as described above in connection with the '071 patent, a POSA viewing the purity and dosing specifications would not have known that the inventors actually invented D-Asn daptomycin. *See supra* ¶ 115-118.

162. Some of the asserted claims (*e.g.*, dosing) are method claims. But "whether a compound is claimed *per se* or a method is claimed that entails the use of the compound, the inventor cannot lay claim to that subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds." *Univ. of Rochester v. G.D. Searle & Co*, 358 F.3d 916, 926 (Fed. Cir. 2004). And as explained above (¶ 115-118), and Dr. Gerwick admitted, Cubist cannot meet this standard. Thus, for the same reasons discussed above, the purity and dosing patents violate the written description requirement.

B. The Construction Of The Claim Term "Daptomycin" Should Be Revised To Reflect The Evolution Of The Law And The Facts.

163. Although it has construed the term "daptomycin," the Court may and should revise its construction if appropriate "as its understanding of the technology evolves." *Greatbach*, 599 F.3d at 1316. Since the Court's *Markman* ruling, both the facts and the law have evolved. The Federal Circuit has issued an indistinguishable decision (*Bayer*), changing the law, and one of this Court's key factual findings urged by Cubist was disproven at trial, changing the facts.

164. The Federal Circuit's ruling in *Bayer* is on all fours. As the Court confirmed, "it is hardly unknown for a patentee with an invention that could be protected to fail in securing such protection by bad choices in claim drafting." 728 F.3d at 1332. This is especially true

where, as here, the patentee has an "initial mistaken belief" about a scientific point, but then "insist[s] on" taking no steps to fix the resulting claim "even after it was known to be false." *Id.*

165. *Bayer*'s facts are strikingly similar. There, as here, the patentee (1) included a scientific mistake in its patent claims; (2) learned of its mistake during prosecution, but did nothing to fix it; and (3) then attempted instead to fix the mistake through claim construction. The claim term at issue in *Bayer* was "having the biological activity of 2,4-D monooxygenase." *Id.* at 1326. But as scientists discovered before the patent issued, "it was incorrect to refer to Bayer's enzyme as a monooxygenase" because it "was … a dioxygenase." *Id.* Bayer knew this, but did nothing address the problem during prosecution. The Federal Circuit construed "monooxygenase" according to its "accepted scientific meaning" as of the filing date—thus warning patentees not to sit idly in the face of a new discovery (728 F.3d at 1328-29):

> Bayer chose the language based on an unverified belief that it accurately described its enzyme, learned that the belief was false while its application was pending, had seven years before its patent issued to alter the language, but never did.

166. When filing its original patent application, Cubist relied on a similarly widespread belief: that daptomycin contained L-Asn. *Supra* ¶ 90. In the dosing patents, for instance, Cubist represented that "[d]aptomycin is described in Baltz" and directed readers to "FIG 1a, Baltz," which of course depicts L-Asn daptomycin. DTX-014, col. 1 ln. 40-47; DTX-268 at 417 (Baltz). Like Bayer, Cubist could have verified its belief that the molecule included L-Asn before its patents issued, given that all the tools to do so were available as far back at 1987 (*supra* ¶¶ 94-96)—which is directly contrary to this Court's *Markman* finding (urged by Cubist) that scientists discovered the truth "using new technology." D.I. 59 at 2 n.1.

167. Also like Bayer, Cubist discovered its mistake during prosecution, yet did nothing to fix it during prosecution. It determined the correct stereochemistry in 2001 (*supra* ¶ 97)—over a year before the first patent originally issued. But Cubist never revised its claims to clarify

that daptomycin meant D-Asn daptomycin and not L-Asn daptomcyin. Although it has now done so successfully *after* patent issuance—through claim construction—Cubist never attempted *before* issuance to convert its claims to product-by-process claims, such as by adding the process limitation the Court has now adopted, *i.e.*, the "antibiotic derived from the fermentation of Streptomyces roseoporus." D.I. 59 at 1. Cubist should not be permitted to fix its claims retroactively.

168. During *Markman*, Cubist overcame the law barring addition of process limitations on the strength of a false "equitable" appeal—that "new technology" was required to find the old error. But this argument does violence to the settled rule that claims are construed as a POSA would understand them "at the time of the invention, i.e., as of the effective filing date." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (en banc).

169. Using that date-restriction, the Court must essentially engage in *time travel*, completely ignoring the later-discovered mistake that the "L" really should be a "D." This exposes the flaw in the results-oriented approach advocated by Cubist. As of 2000—the last priority date for these four patents—nobody would have even proposed, much less adopted, a process limitation for the original claims. There would have been no reason to do so, because nobody would have known to advocate such an unconventional claim construction. The scientists who discovered daptomycin tried to determine the stereochemistry, and they believed they were right. *See supra* ¶ 95. Cubist should not now be allowed to inject the benefit of hindsight into the claims.

170. In sum, Hospira respectfully submits that this Court should revise its construction of "daptomycin" to reflect what everyone believed in 2000: "daptomycin" contained L-Asn. Under that construction, there is no dispute that Hospira does not infringe any of the asserted patents.

CONCLUSION

171. For the foregoing reasons, the asserted claims are invalid, not infringed, or both.

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